



Universitäres Herzzentrum
Hamburg

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***26. Bielefelder Seminar über aktuelle Fragen in der Kardiologie 07.02.2009
„Von der Prophylaxe zur Therapie kardialer Erkrankungen - was gibt es Neues ?“***

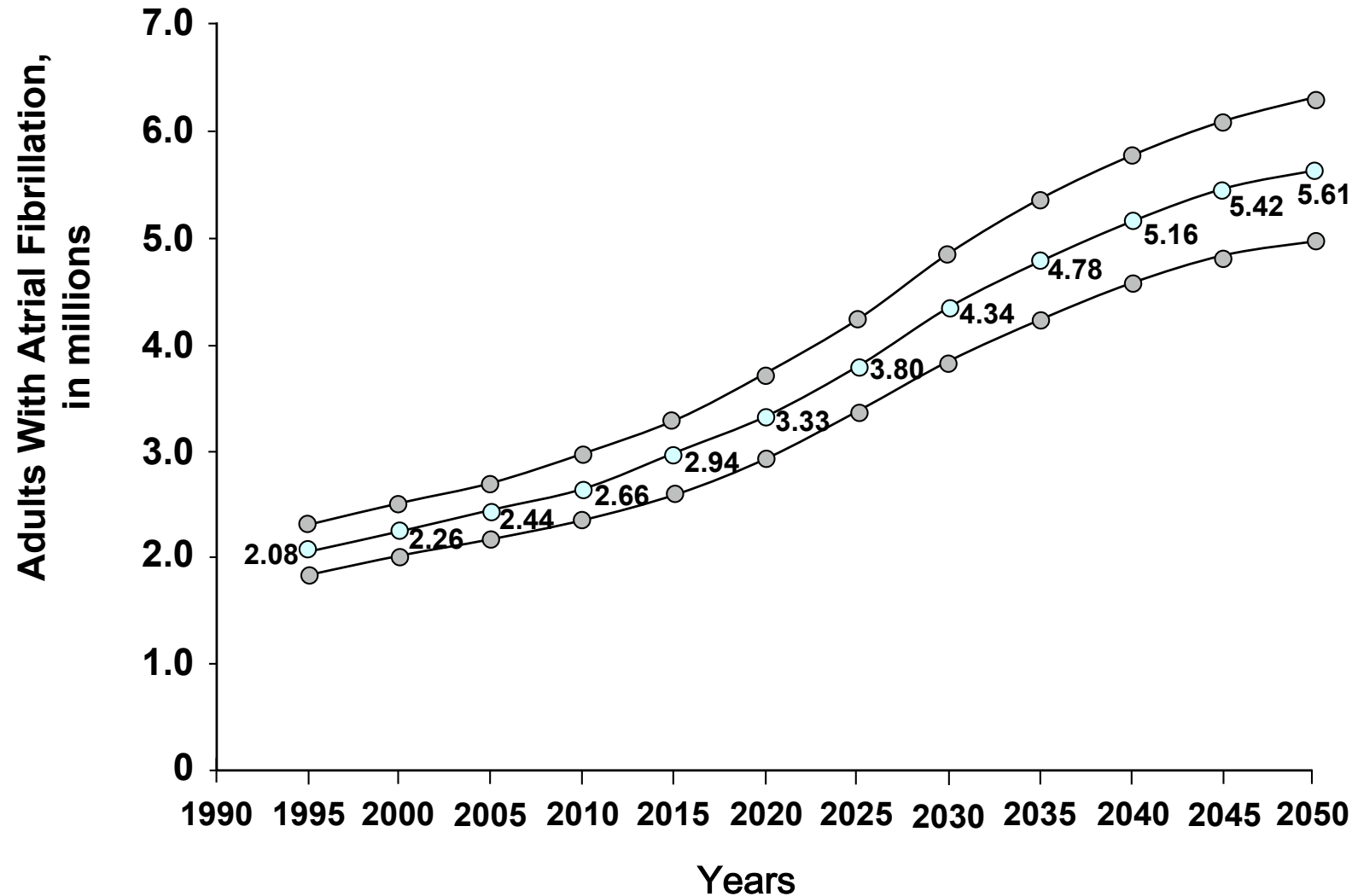
Aktuelle Therapie des Vorhofflimmerns: Bericht aus dem Kompetenznetz Vorhofflimmern

Stephan Willems

Klinik für Kardiologie mit Schwerpunkt Elektrophysiologie

Universitäres Herzzentrum Hamburg

Entwicklung der Prävalenz von Vorhofflimmern (USA)





Die Therapie der Flimmerarrhythmie gehört zu den dankbarsten Aufgaben. Praktisch kommt man mit zwei Gruppen von Medikamenten aus, den Digitalispräparaten und den Chininpräparaten, insbesondere dem von *Frey* in die Therapie eingeführten Chinidin. Eine Ausnahme macht scheinbar nur das Vorhofflimmern bei Hyperthyreosen, das in der thyreotoxischen Situation sich refraktär gegen beide Medikamente verhält, dagegen ansprechbar auf diese nach der Strumektomie wird.

THEODOR BRUGSCH / KARDIOLOGIE
LEHRBUCH DER HERZ- UND GEFÄSSKRANKHEITEN
zugleich eine Pathologie des Kreislaufs

4. Auflage

(1954)



ACC/AHA/ESC Practice Guidelines

ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation—Executive Summary

**A Report of the American College of Cardiology/American Heart Association
Task Force on Practice Guidelines and the European Society of Cardiology
Committee for Practice Guidelines (Writing Committee to Revise the 2001
Guidelines for the Management of Patients With Atrial Fibrillation)**
*Developed in Collaboration With the European Heart Rhythm Association and the Heart
Rhythm Society*

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Consensus Statement 2007

HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Personnel, Policy, Procedures and Follow-Up: A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA) and the European Cardiac Arrhythmia Society (ECAS); in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS).

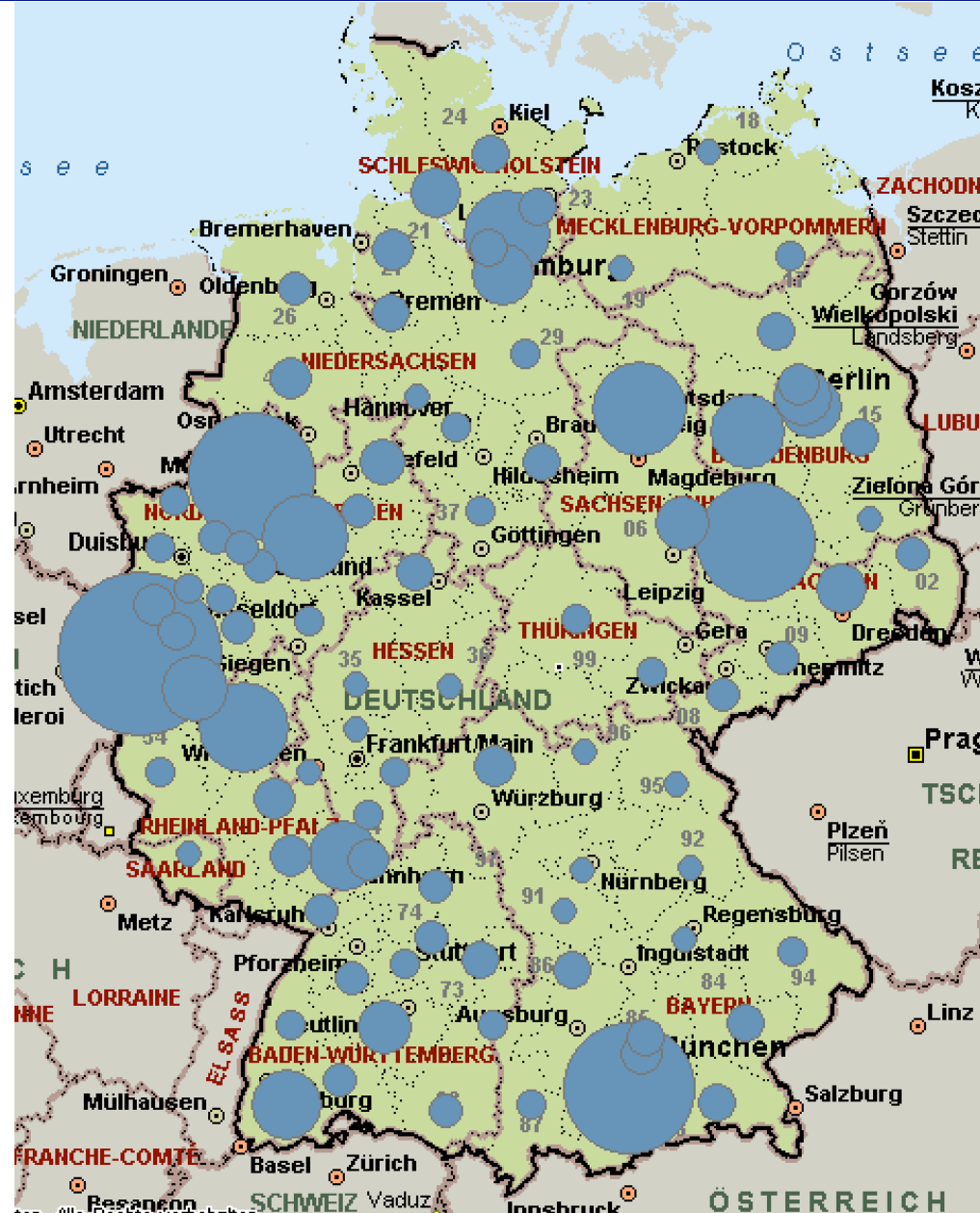
Endorsed and Approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society



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Kompetenznetz Vorhofflimmern



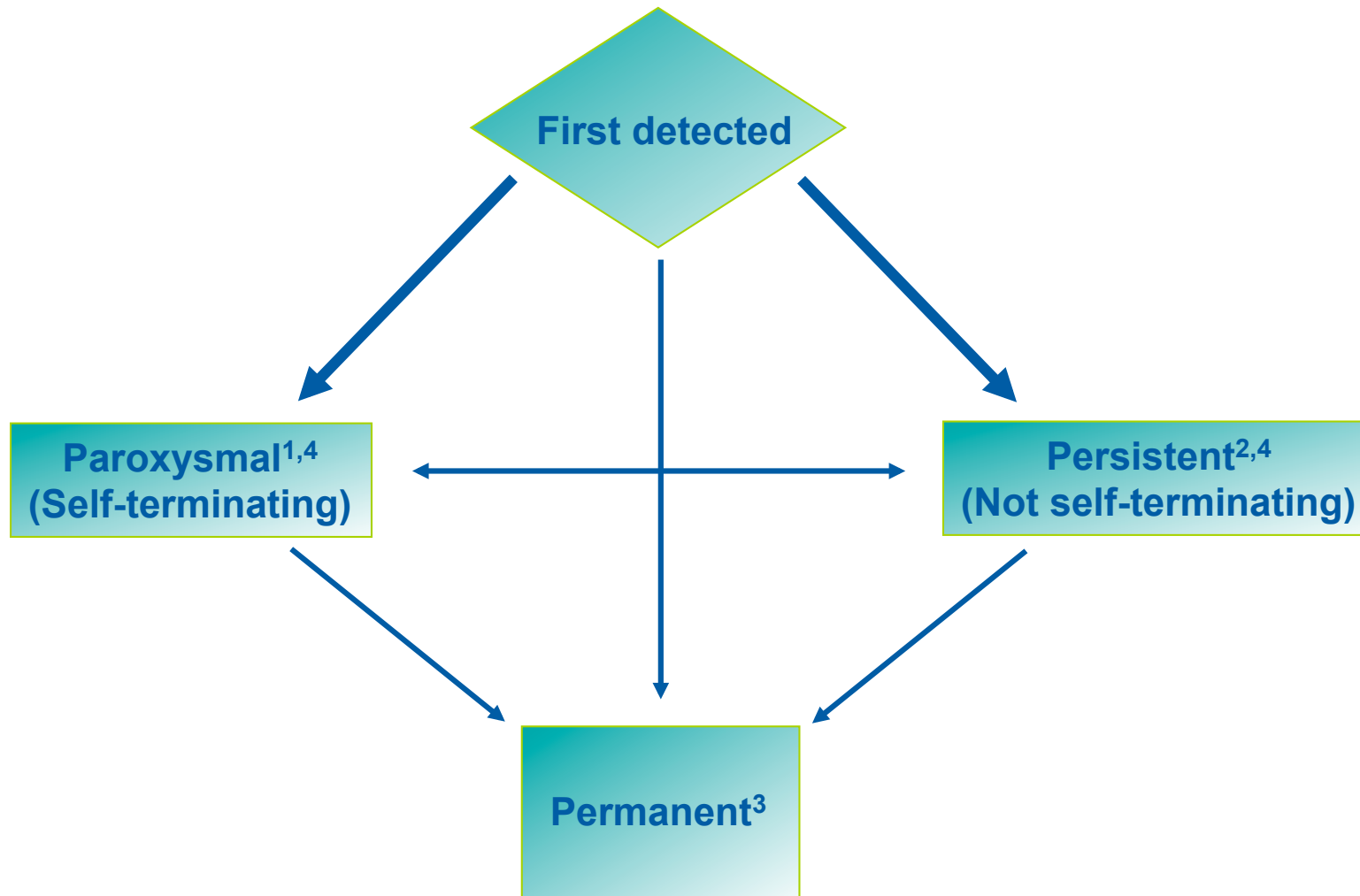
German AF Net 2008



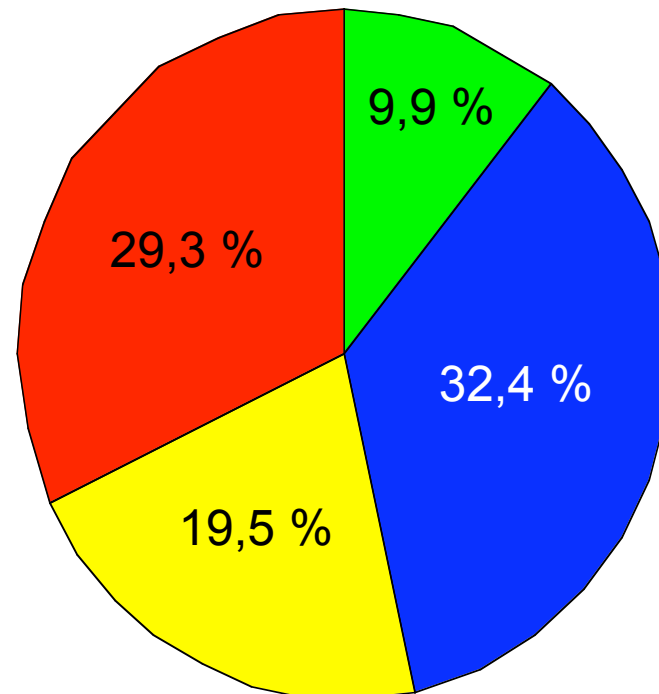
- Grundlagen
 - Def., Klass., Epidem., Pathophys., QOL, Eval.,
- Management
 - Strategien („Strategic Objectives“)
 - Rhythmus vs. Frequenzkontrolle
 - Prävention von Thrombembolien
 - Medikamentöse (DC) Kardioversion
 - Substanzen zur medikamentösen Rhythmuskontrolle
 - Erhalt des Sinusrhythmus
 - Medikamentöse Therapie
 - Nicht-medikamentöse Therapie



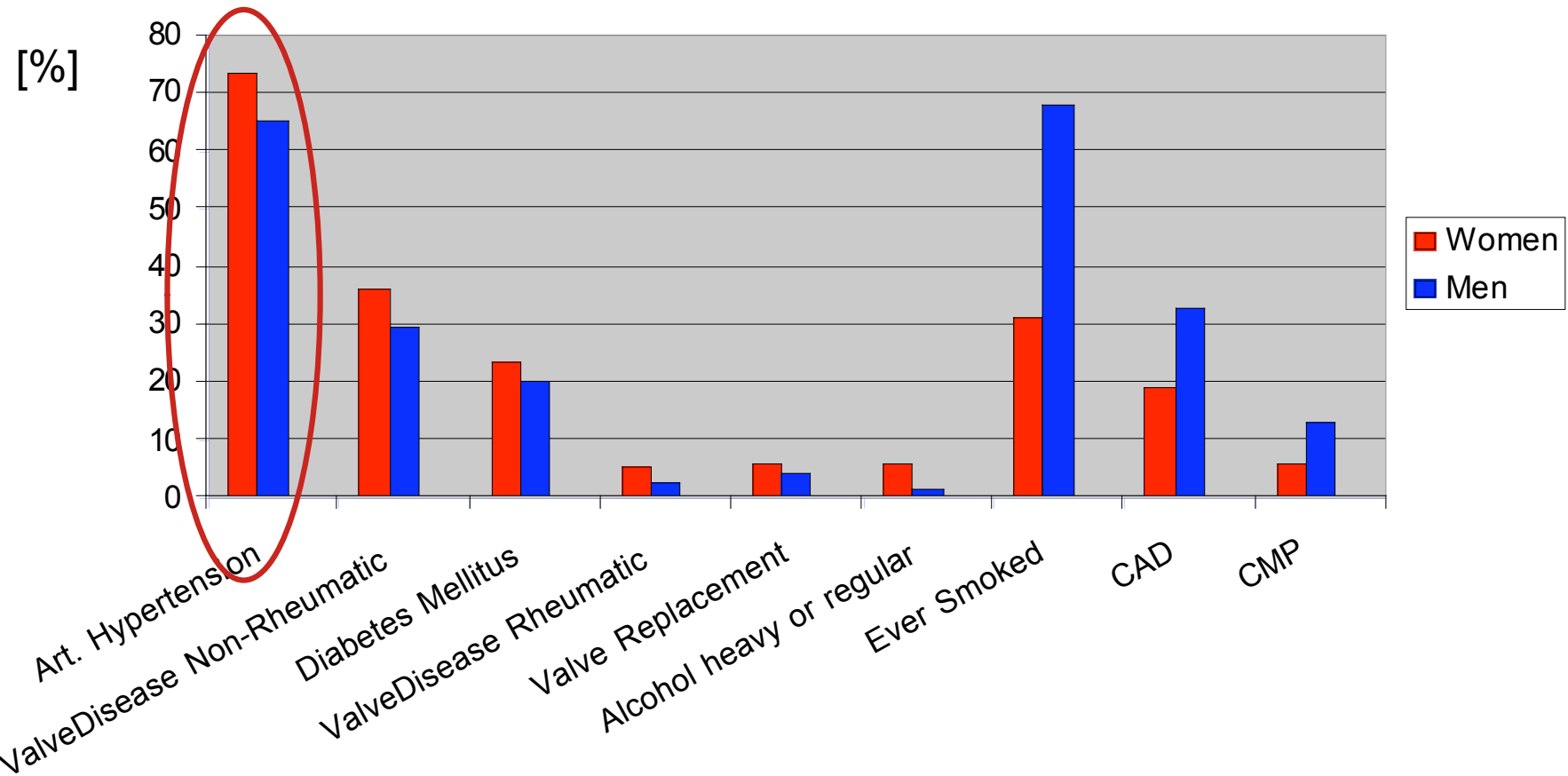
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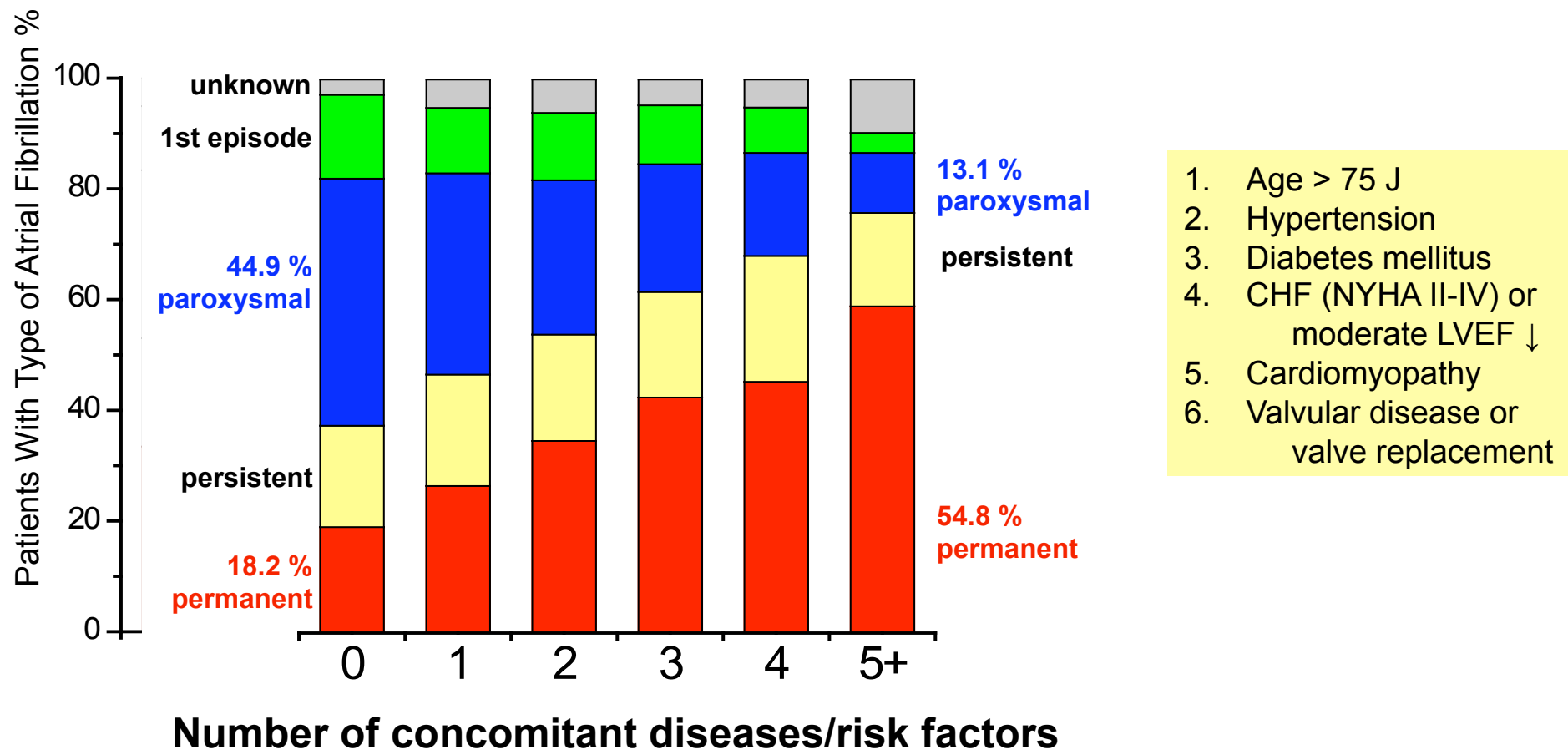
(based on a population of 9551 pts.)



- 1st episode
- Paroxysmal
- Persistent
- Permanent



Distribution of AF type regarding concomitant diseases/risk factors





- Grundlagen
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Rhythmus- oder Frequenzkontrolle ?

Studie	Patienten	Primärer Endpunkt
PIAF	252	Lebensqualität, Symptomatik
STAF	200	Mortalität, Thromboembolie
AFFIRM	4060	Mortalität
RACE	522	kardiovaskuläre
Morbidität,		Mortalität

Fazit:

***Frequenzkontrolle ist der Rhythmuskontrolle
nicht unterlegen !***



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A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

ABSTRACT

Background There are two approaches to the treatment of atrial fibrillation: one is cardioversion and treatment with antiarrhythmic drugs to maintain sinus rhythm, and the other is the use of rate-controlling drugs, allowing atrial fibrillation to persist. In both approaches, the use of anticoagulant drugs is recommended.

Methods We conducted a randomized, multicenter comparison of these two treatment strategies in patients with atrial fibrillation and a high risk of stroke or death. The primary end point was overall mortality.

ATRIAL fibrillation is the most common sustained cardiac arrhythmia, yet the optimal strategy for its management remains uncertain.¹⁻⁴ During atrial fibrillation, most symptoms (but perhaps not all) are caused by a poorly controlled or irregular ventricular rate, and the associated risk of death is doubled in patients who have a history of atrial fibrillation.⁵⁻¹⁰ Although adequate anticoagulation with warfarin substantially lowers the risk of stroke,¹¹⁻¹³ this drug is frequently not administered.¹⁴

TABLE 2. Covariates Significantly Associated With Survival Results With Echocardiographic Data Included

Covariate	P	HR	HR: 99% Confidence Limits	
			Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

*Per year of age.



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Rhythm Control versus Rate Control
for Atrial Fibrillation and Heart Failure

Hypothese: „a rhythm-control strategy would reduce the rate of death from cardiovascular causes, as compared with rate-control strategy...in pts. with AF and heart failure“

Einschlusskriterien:

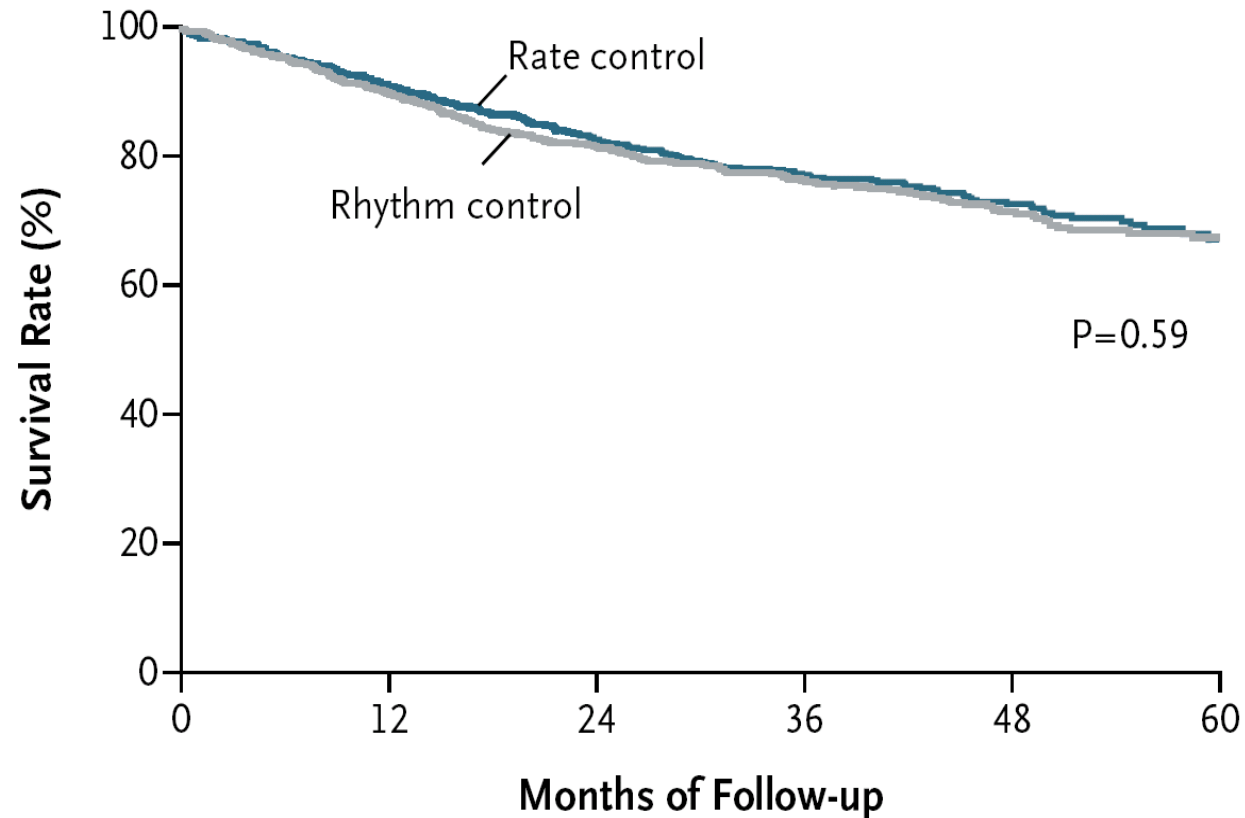
- LVEF \leq 35%
- symptomatische HI NYHA II – IV

(alternativ: NYHA I, aber LVEF < 25% und

Hospitalisierung wegen HI)

- Vorhofflimmern

Death from Cardiovascular Causes (Primary Outcome)

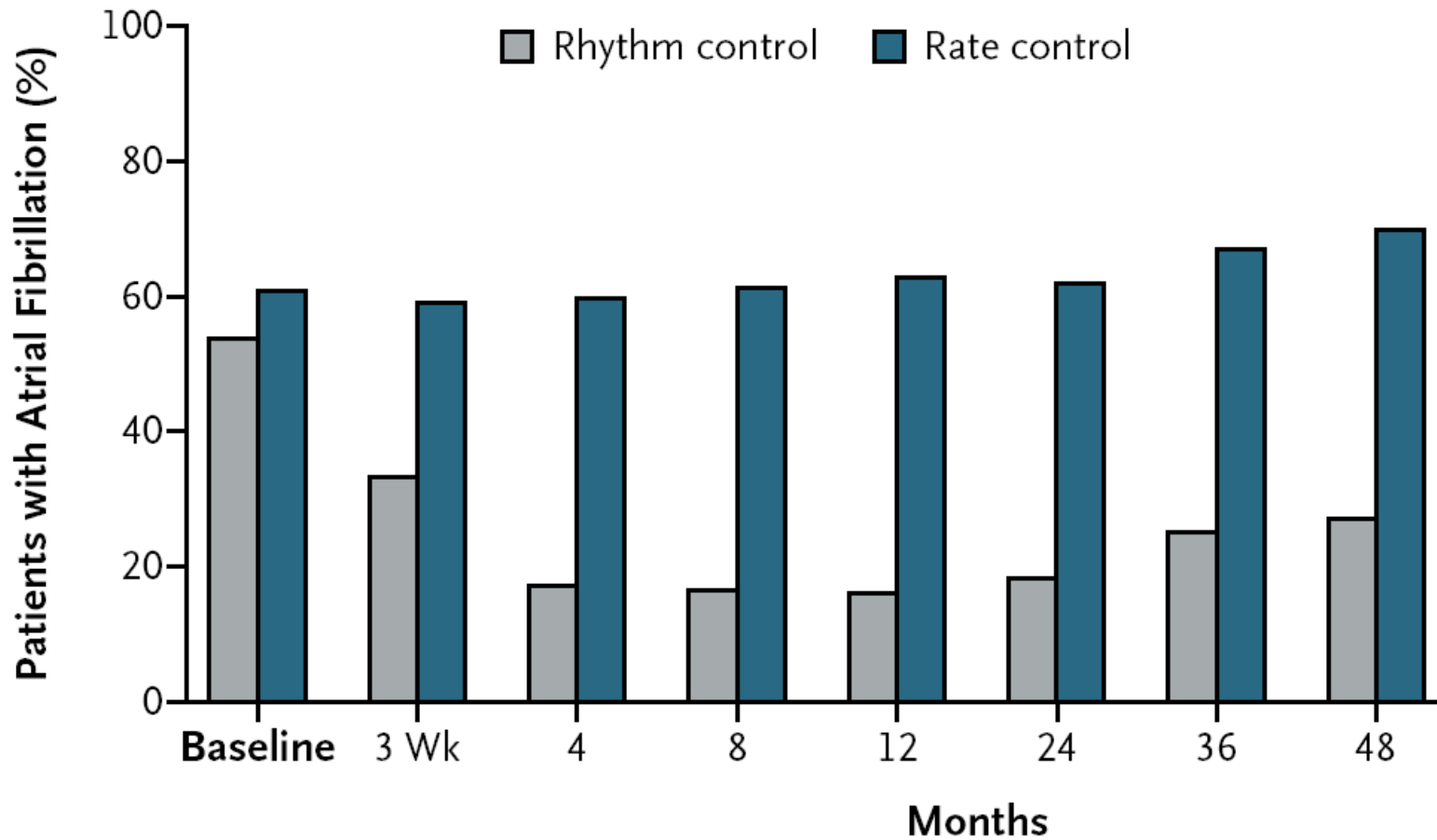


No. at Risk

Rhythm control	593	514	378	228	82
Rate control	604	521	381	219	69

Rhythmus- oder Frequenzkontrolle ?

A Follow-up Visits





Frequenz- oder Rhythmuskontrolle ?

“...rate control may be reasonable initial therapy in **older patients** with persistent AF who have hypertension or heart disease.

For **younger** individuals, especially those with paroxysmal lone AF, rhythm control may be a better initial approach.... **catheter ablation** should be considered to maintain SR in selected patients who failed to respond to AA tx ”

Sinusrhythmus ist „besser“ als Vorhofflimmern - auch in prospektiven Studien ?!

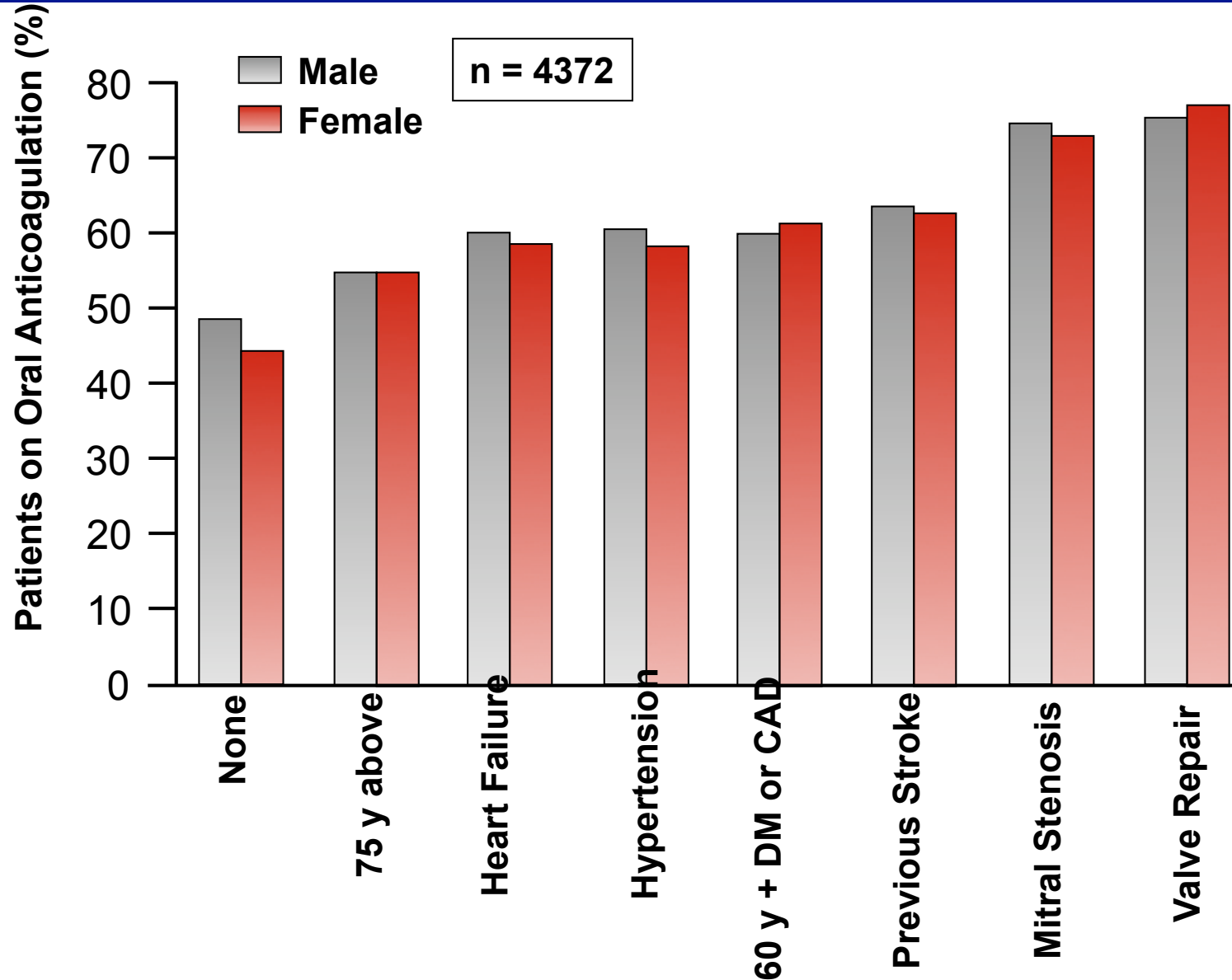


Potentielle Folgen von pers. AF:

- o LA Dilatation
- o Konsekutive (funktionelle) Mitralinsuffizienz
- o Reduzierte LV-Funktion => Herzinsuffizienz



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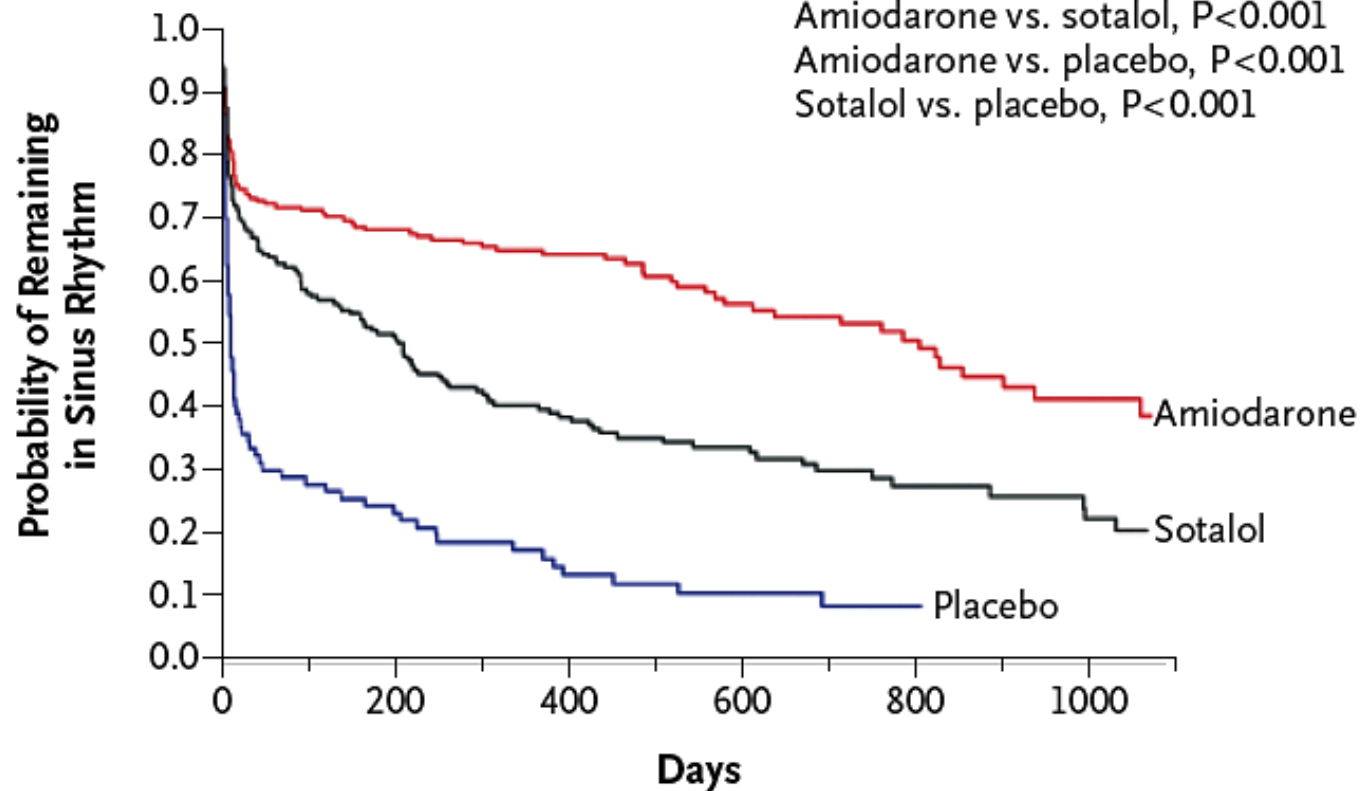




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SAFE-T-Studie

All Patients



No. at Risk

Amiodarone	206	131	98	60	38	18
Sotalol	195	97	61	38	21	13
Placebo	90	21	11	8	5	2

Nebenwirkungen von Amiodaron ($n=6500$):

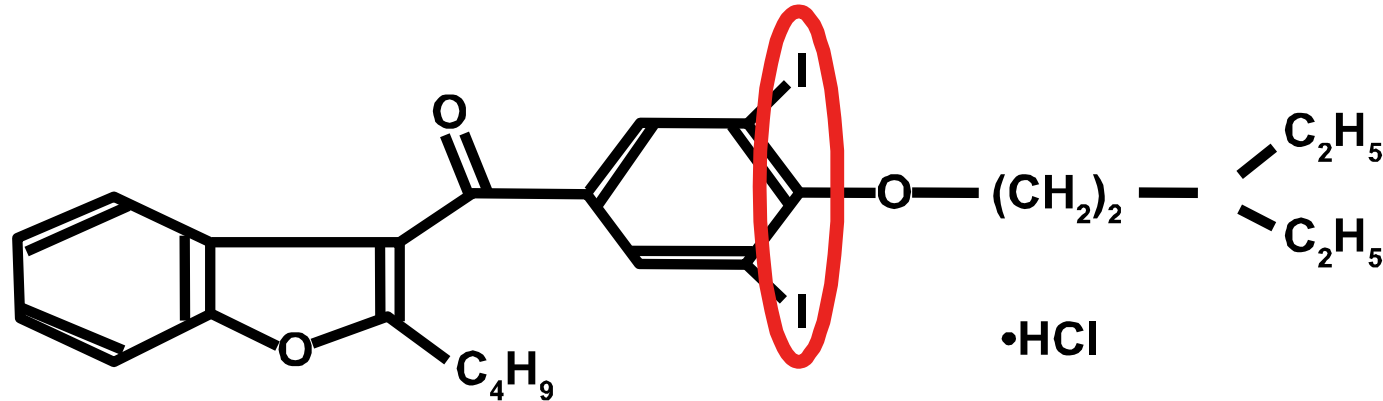
Kardial

- Proarrhythmie: < 1%
- Bradykardie: < 2%
- Hypotonie: (selten)

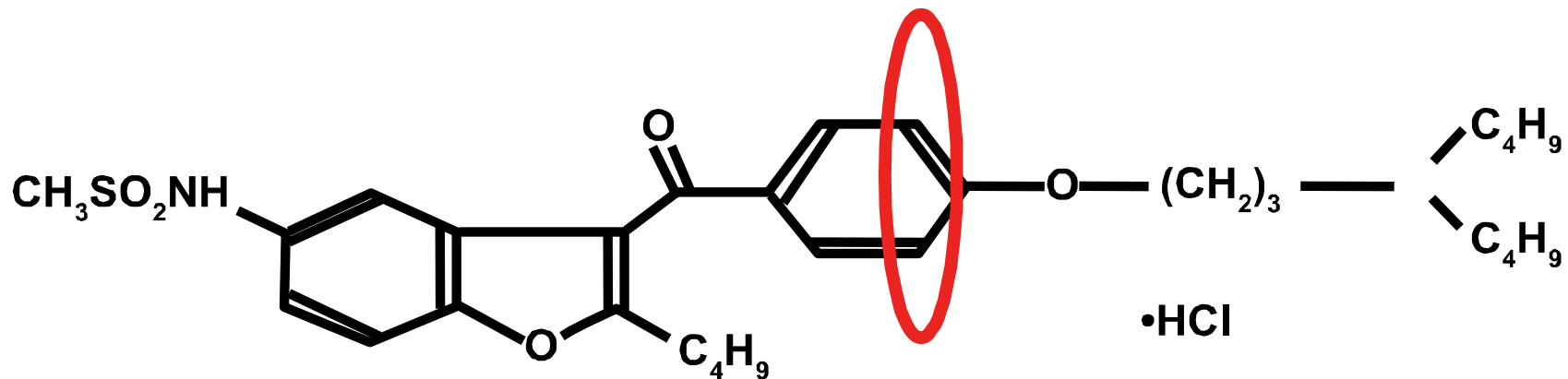
Extrakardial

- SD-Funktionsstörungen: ~ 8 %
- Hautveränderungen: ~ 5 %
- Lungentoxizität: ~ 1 %
- Kornea-Ablagerungen: ~ 1 %
- Hepatotoxizität: < 1 %
- Periphere Neuropathie: 0,3 %

Dronedarone, a non-iodinated Amiodarone Derivative



Amiodarone (MW = 682)



SR33589B/Dronedarone (MW = 599)

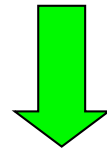


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ATHENA

A Trial with dronedarone to prevent Hospitalization or dEath in patieNts with Atrial fibrillation/flutter



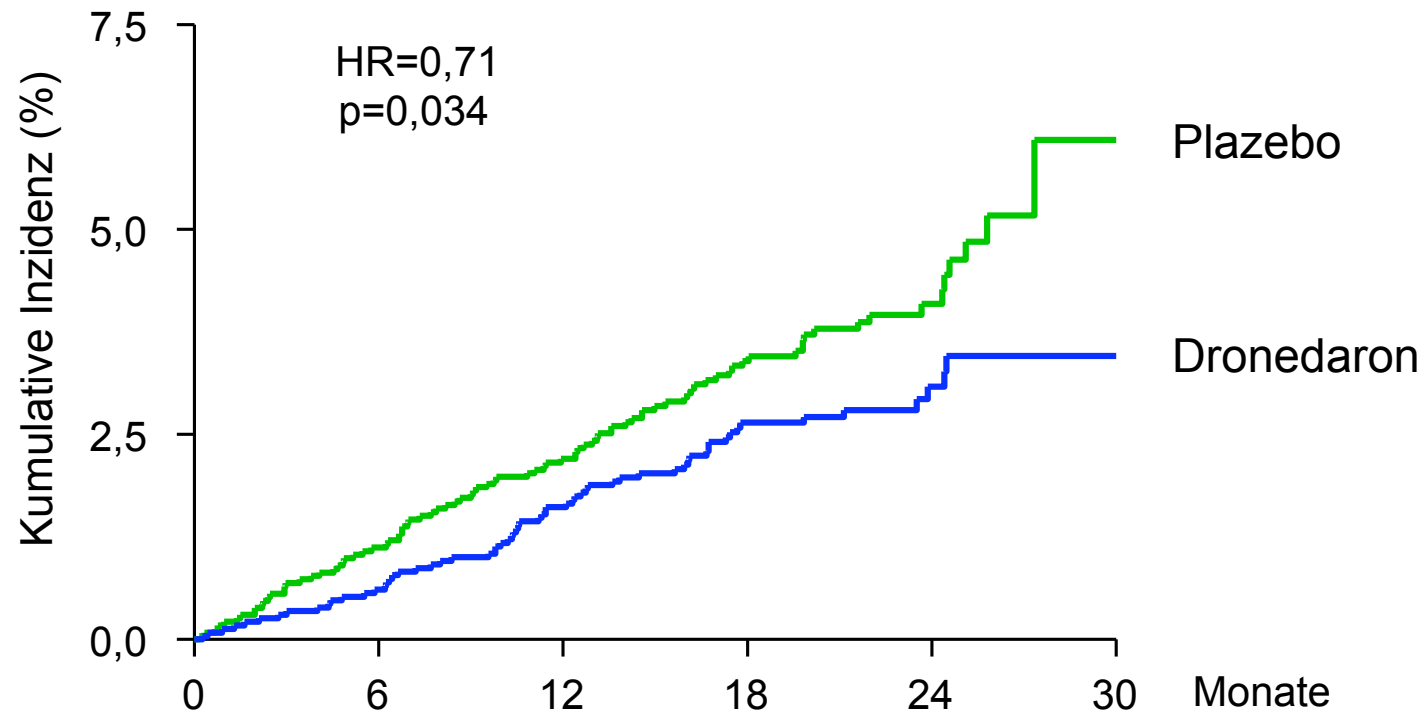
Hypothese:

dronedarone would prolong time to first cardiovascular hospitalization or death in moderate- to high-risk elderly patients with AF
(1 yr follow-up)



ATHENA: Primärer Endpunkt

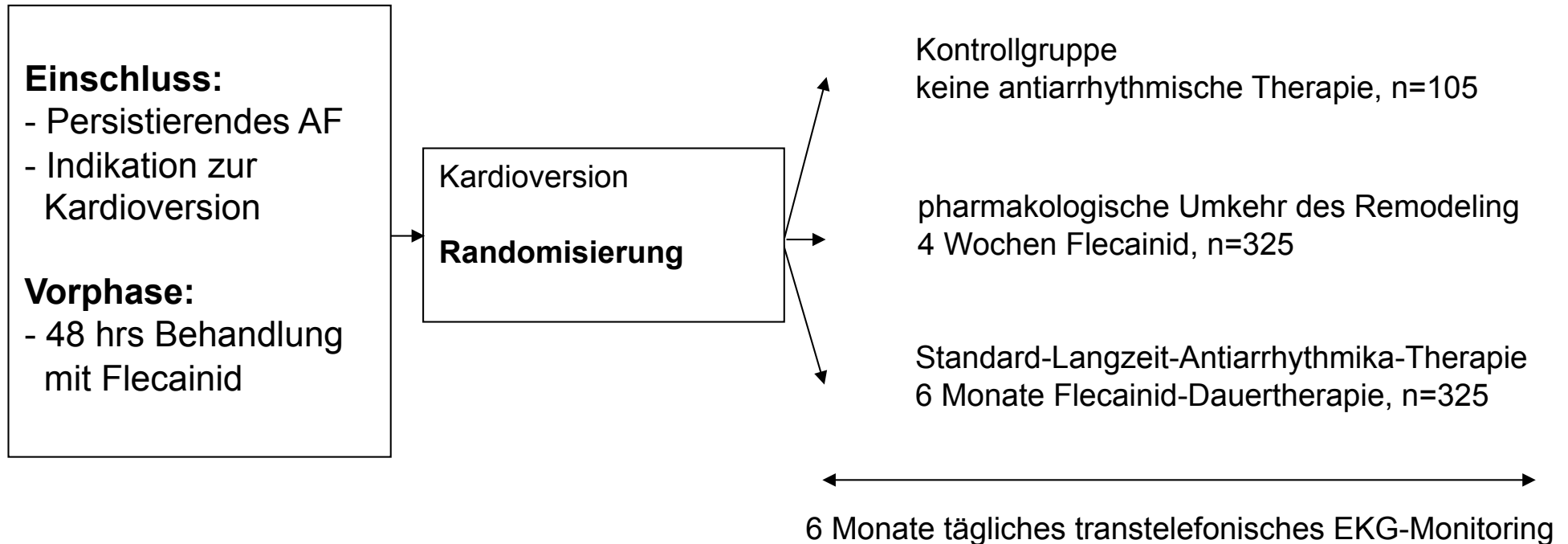
Krankenhausaufnahme aufgrund CV Ursachen oder Tod



Exponierte Patienten

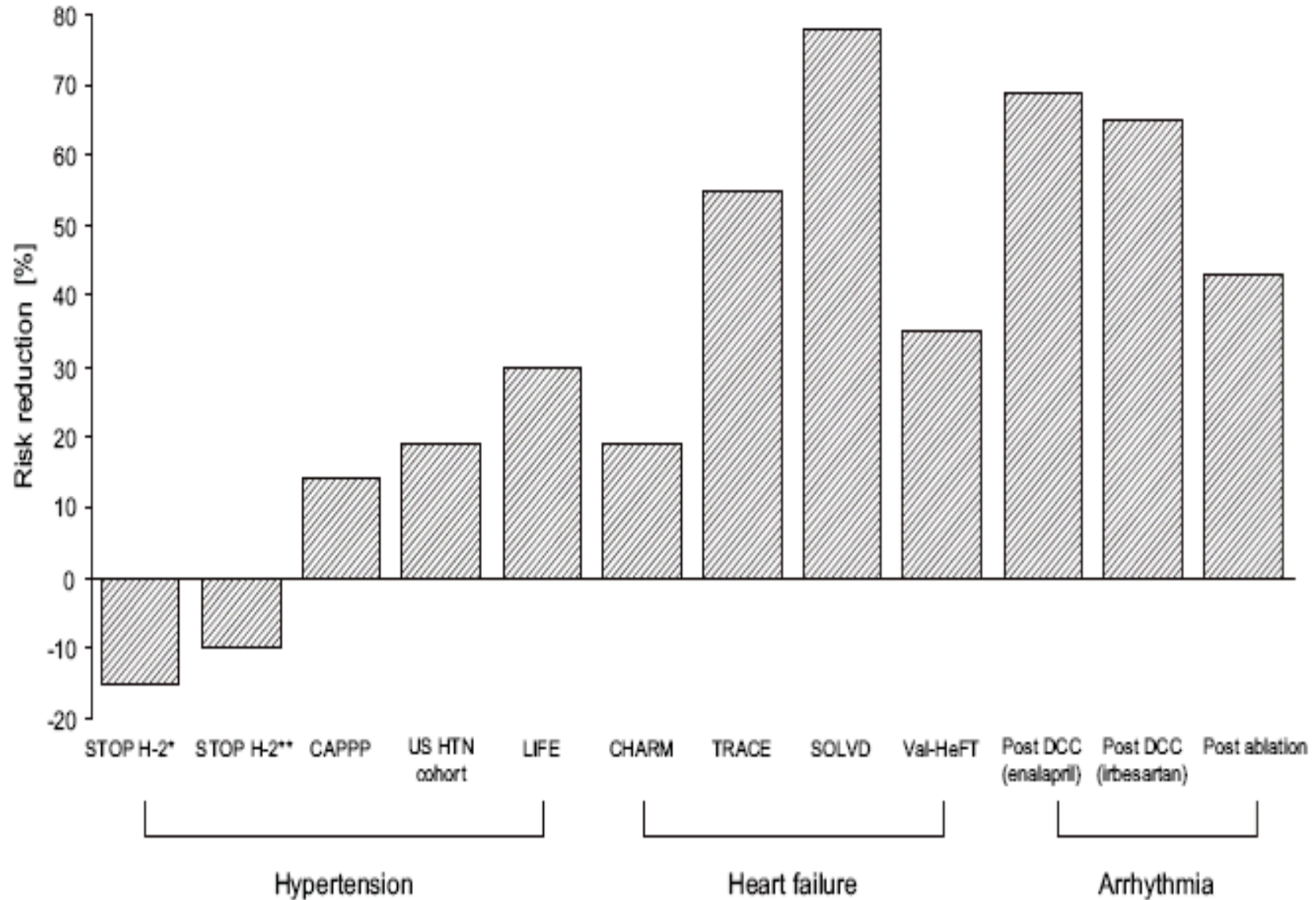
Plazebo	2327	2290	2250	1629	636	7
Dronedaron	2301	2274	2240	1593	615	4

Mittlere Nachbeobachtung 21 ± 5 Monate



- **primäre Hypothese: Eine antiarrhythmische Kurzzeittherapie nach Kardioversion ist genau so effektiv wie die übliche Langzeit-Therapie zur Verhinderung von Vorhofflimmer-Rezidiven**
- **„proof of principle“, Ergebnisse prinzipiell übertragbar auf andere Antiarrhythmika**

AF-Prävention durch ACE/AT₁ Inhibitoren





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AFNET

ANTIPAF

„Angiotensin II-Antagonist in Paroxysmal Atrial Fibrillation Trial“

Prospektive, randomisierte, doppelblinde, multizentrische klinische Studie zur Untersuchung der Wirksamkeit von Olmesartan zur Verringerung von paroxysmalem Vorhofflimmern

PD Dr. A. Goette, Magdeburg
Prof. Dr. T. Meinertz, Hamburg

BMBF-Kompetenznetz „Vorhofflimmern“





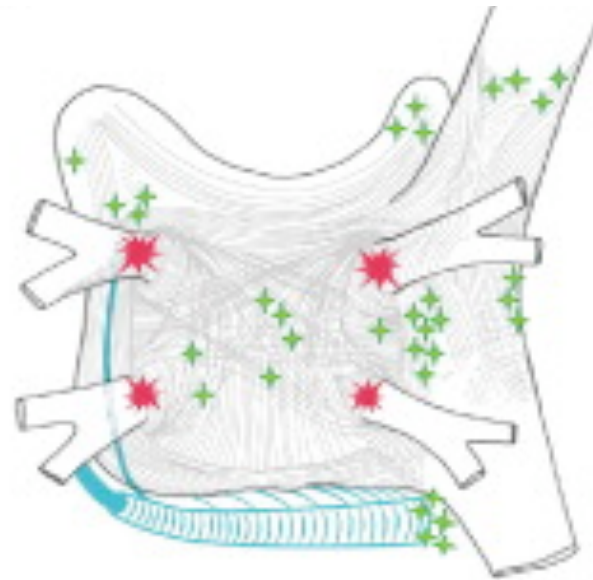
Indication for AF Ablation

- Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication.

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Atrial fibrillation

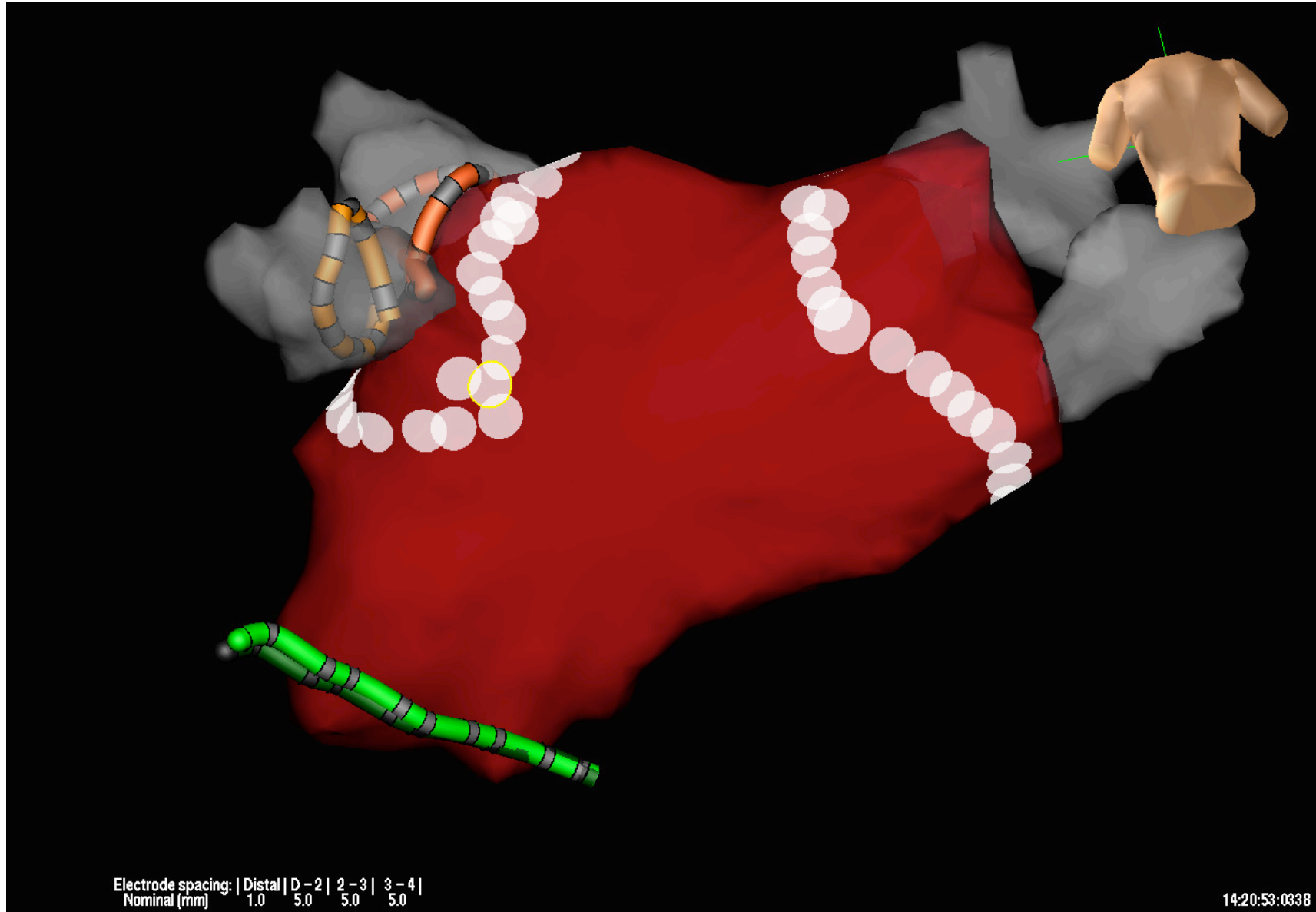
- **paroxysmal**
 - duration hours
 - spontaneous conversion
 - no cardioversions !



mean AFCL ~ 175 ms



Bilateral PV Isolation



Success rates:

Success Rates of Most Recent Studies Using Ablation of All PVs Outside the Tubular Segment

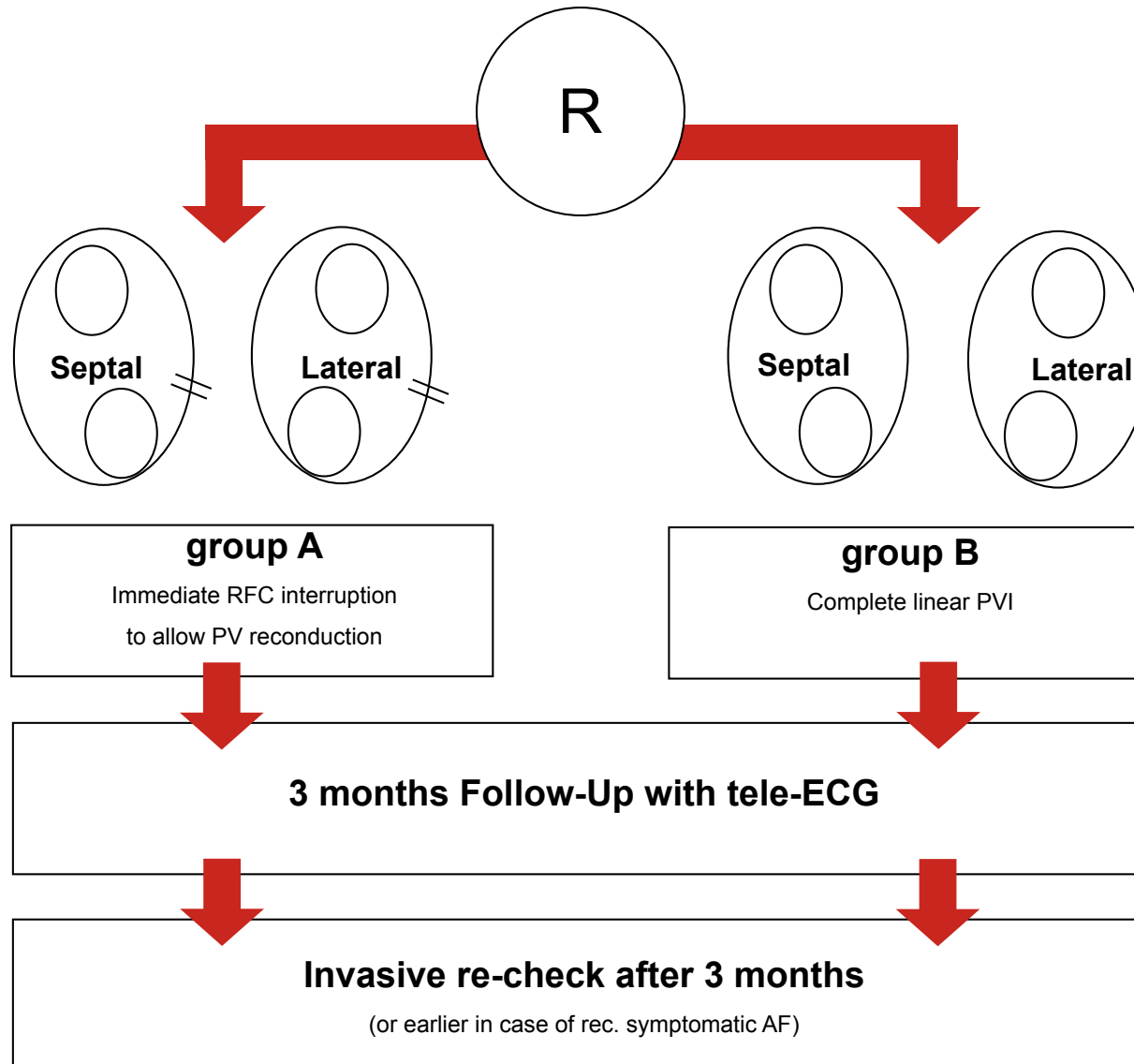
Study	Year	Patients	Age, y	Parox, %	SHD, %	Tool(s)	End Point	AF Free (Off Drugs), %	Follow-Up, d
Ouyang et al ³⁷	2004	41	63±9	100	NA	CARTO	PV Isolat'n	76*	178
Haissaguerre et al ³⁸	2004	70	53±8	NA	43	Fluoro	PV Isolat'n	79	210
Mansour et al ⁴⁰	2004	40	55±10	80	13	CARTO	PV Isolat'n	75	330
Marrouche et al ⁴¹	2003	259	54±11	51	21	ICE	PV Isolat'n	87†	347
Oral et al ³⁹	2003	40	54±11	100	3	CARTO	EGM Red'n	88	365
Pappone et al ³⁶	2003	589	65±9	69	6	CARTO	EGM Red'n	79	861
Total		1039						81.0	

Parox indicates paroxysmal; SHE, structural heart disease; Fluoro, fluoroscopy only; Isolat'n, isolation; and EGM Red'n, reduction of local electrogram amplitude (usually >70%). CARTO is an electroanatomical mapping system (Biosense Webster).

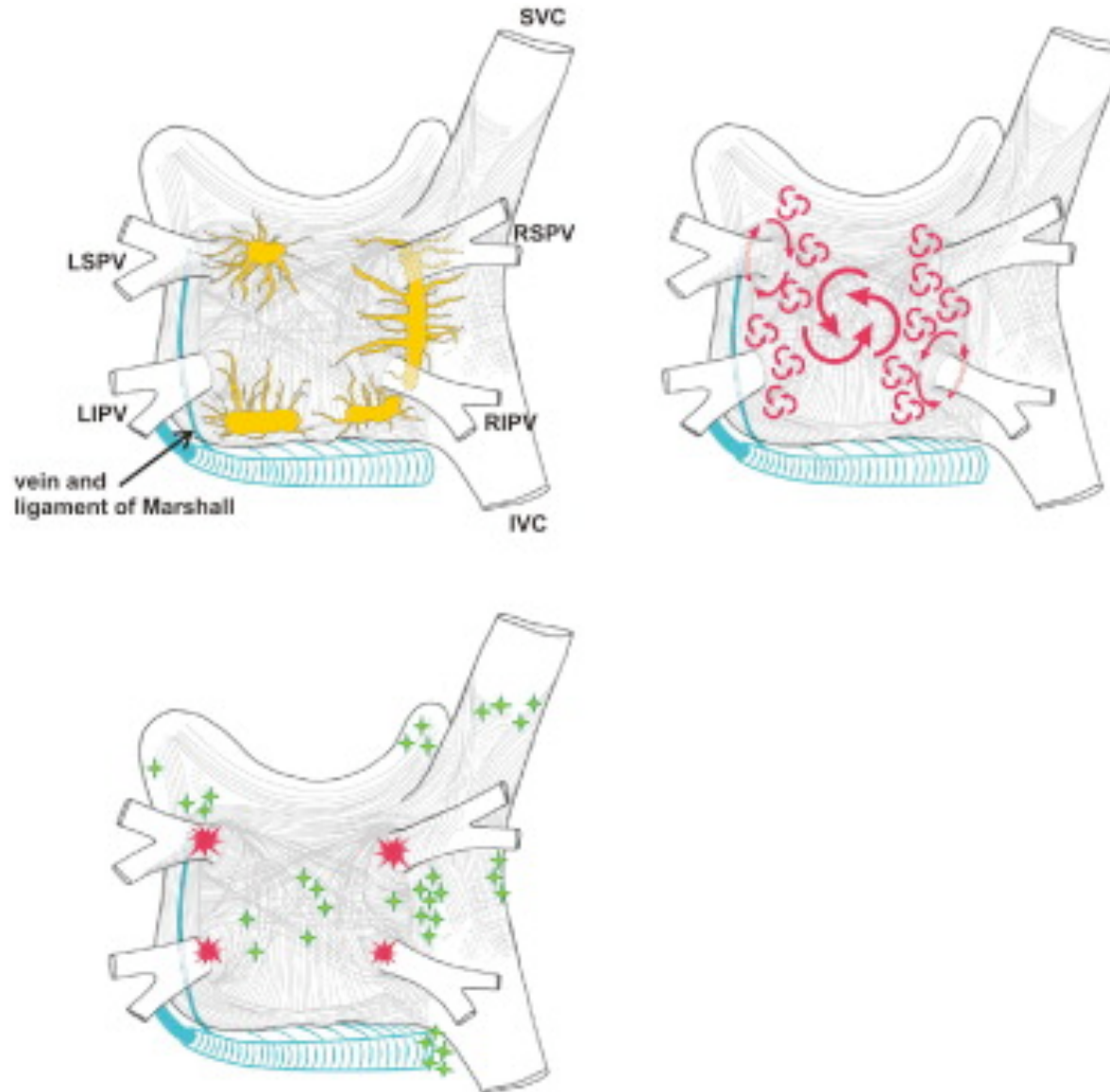
*Success was 95% off drugs after a second procedure.

†Success was 90% off drugs in patients with microbubble monitoring by ICE.

Study flow chart



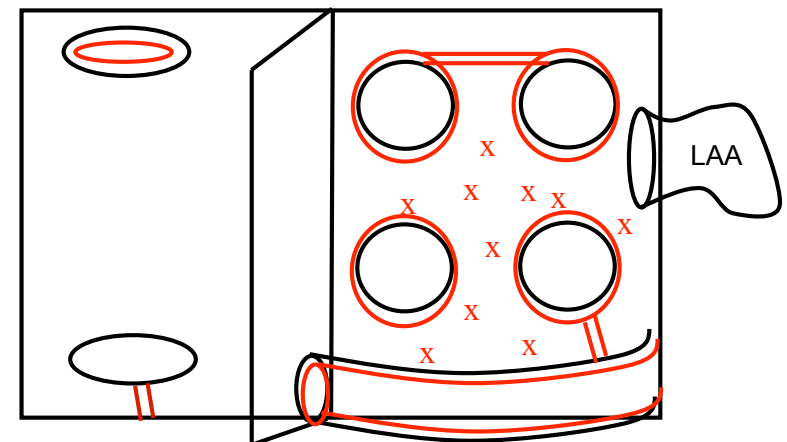
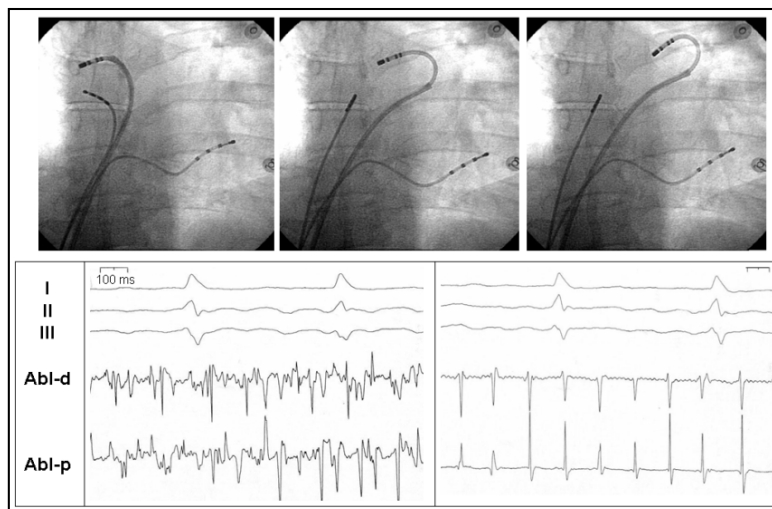
AF Mechanisms



Catheter ablation of chronic AF (n=60, 1.5 years AF)

Ablation Strategy (goal AF Termination !)

- Isolation of all thoracic veins (PVs, CS, SVC)
- atrial defragmentation
- left atrial linear lesions

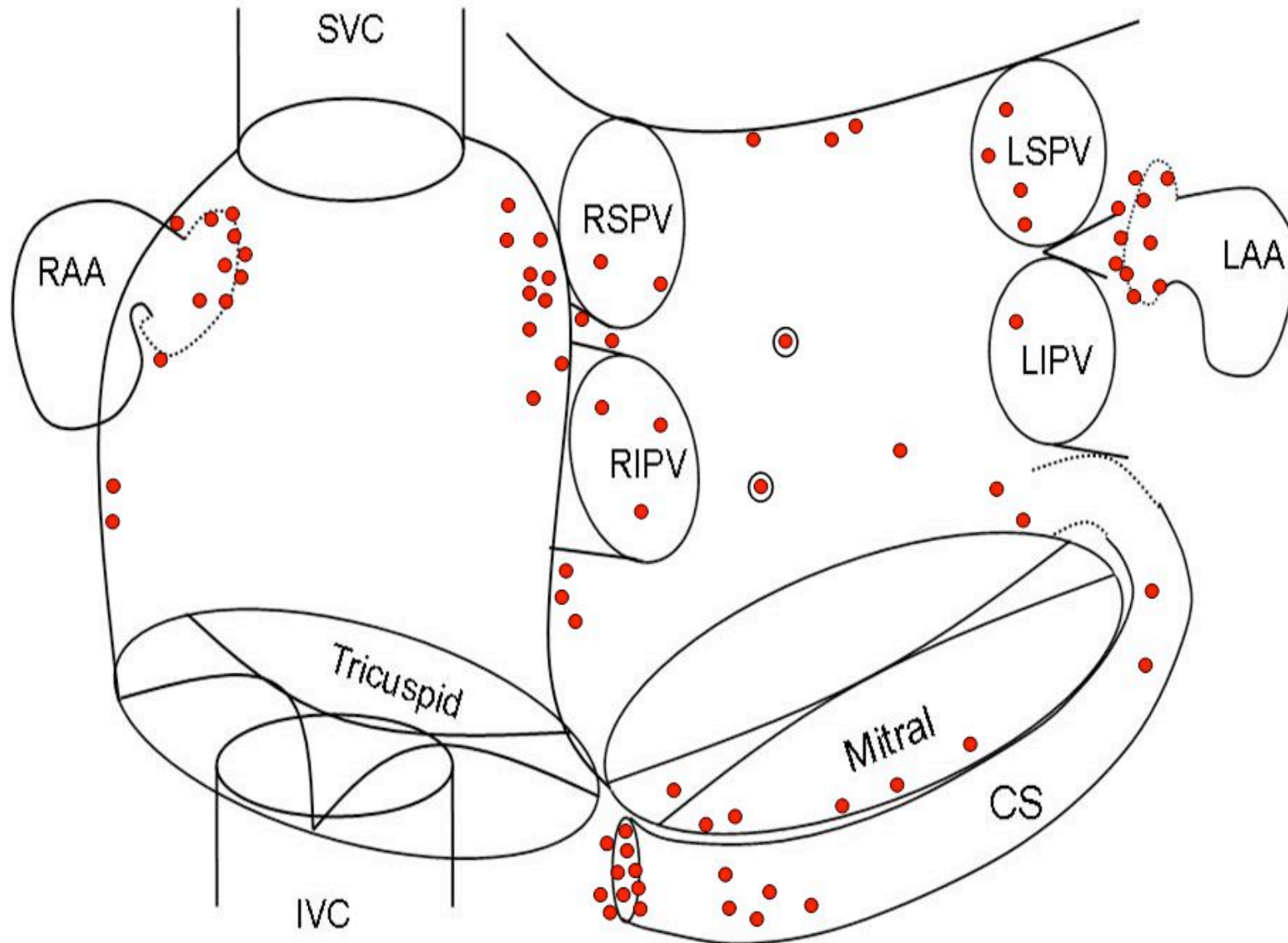




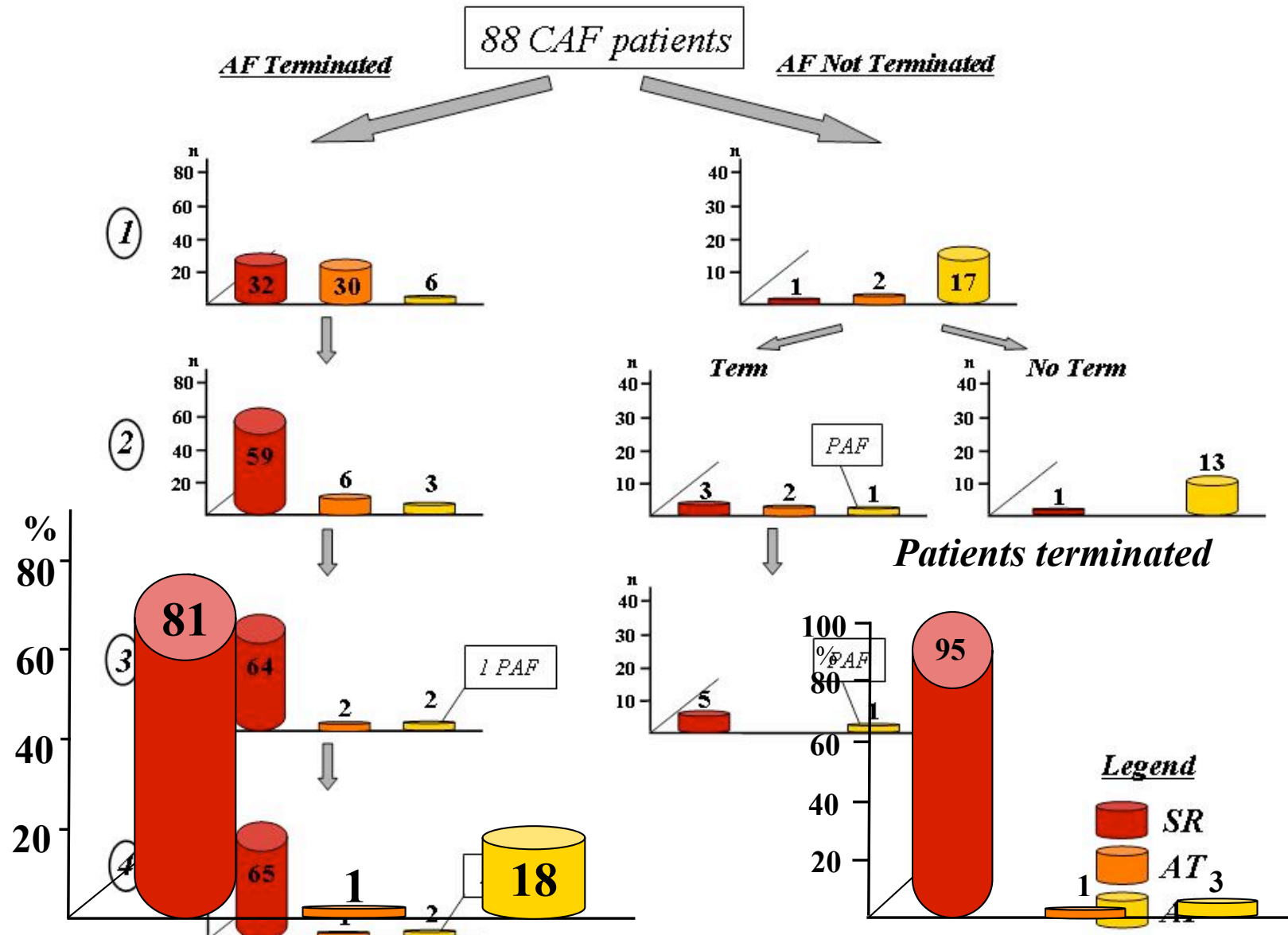
Epidemiological data

- A total number of 88 consecutive patients with chronic AF were included
(all patients with chronic AF referred to our institution for de-novo catheter ablation in 2006)
- mean age: 61 ± 10 years, 11 women
- mean LA diameter: 50 ± 7 mm, mean LVEF: 57 ± 13 %
- mean AF duration: 23 ± 36 months

Sites of CAF termination

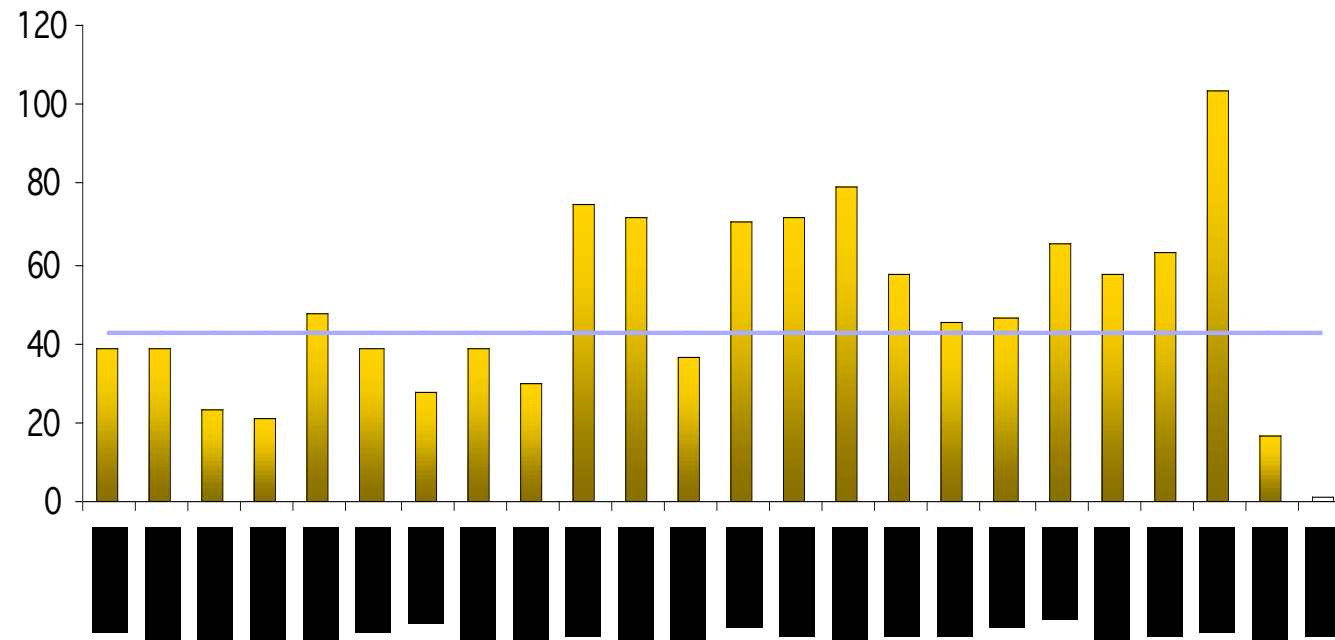


Outcome during FU (18 ± 4 months)





Overall: 1.175 patients
First patient in: 9th January 2006
Last patient in: 7th December 2007





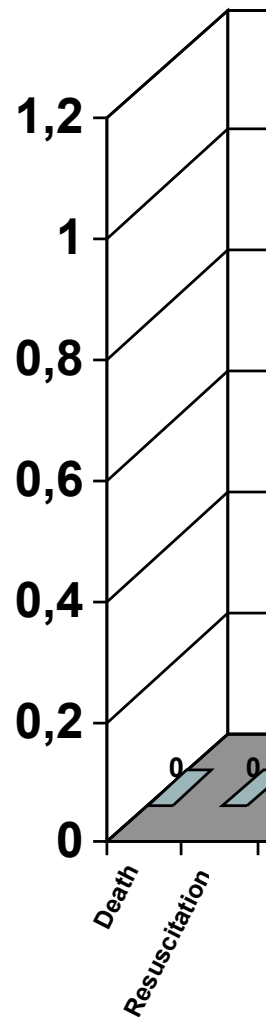
Procedural data



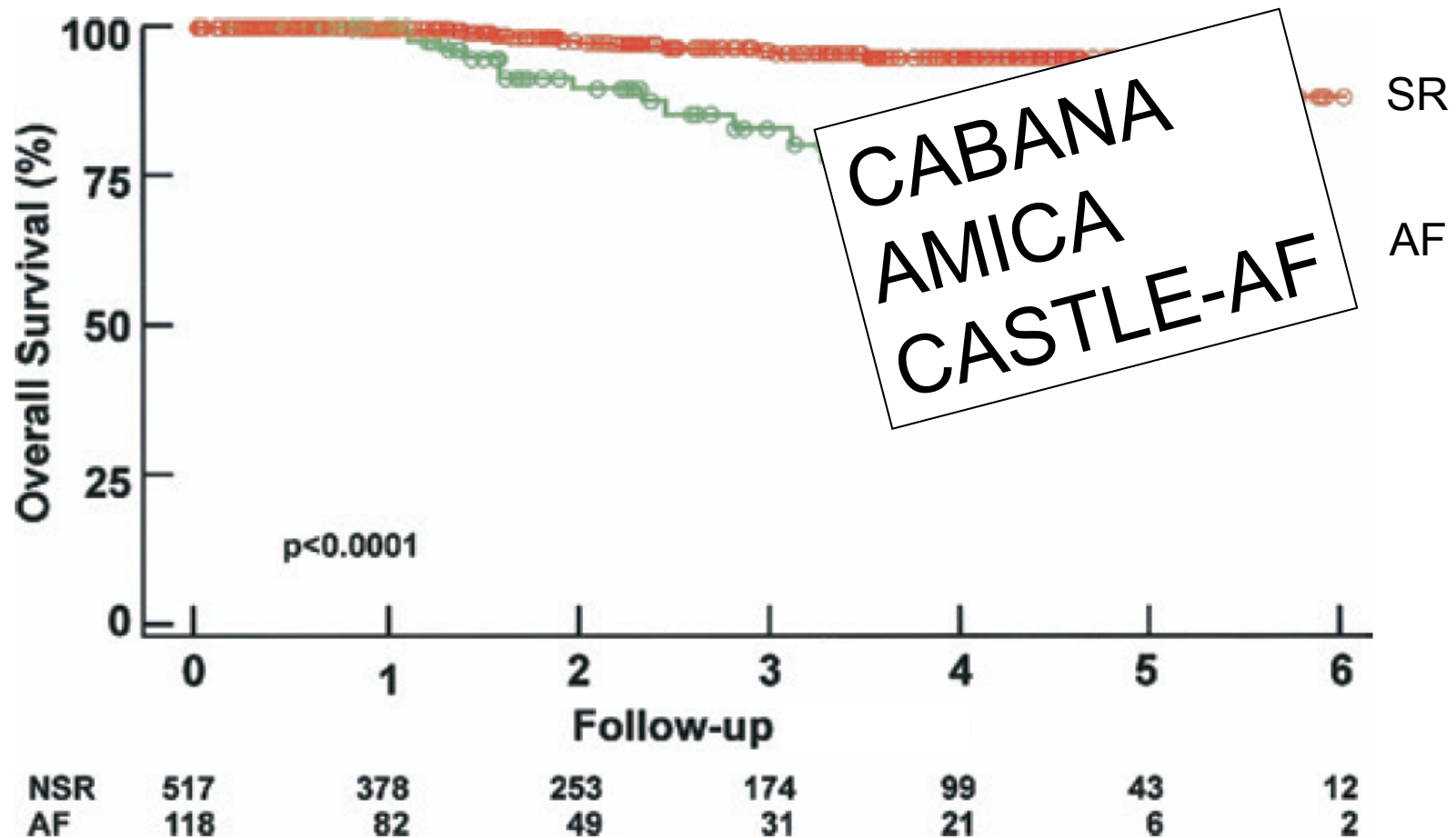
	Female (N = 327)	Male (N = 848)	P Value
<i>Procedural data</i>			
Procedure time [Min.]	190 (150.0-240.0)	200.0 (155.0-255.0)	0.06
Fluoroscopy dose [cGycm²]	585.6 (185.7-3617.5)	646.0 (181.0-4828.0)	0.28
Fluoroscopy time [Min.]	37.0 (24.0-53.0)	38.5 (26.0-59.0)	0.06



Cumulative incidence of major complications

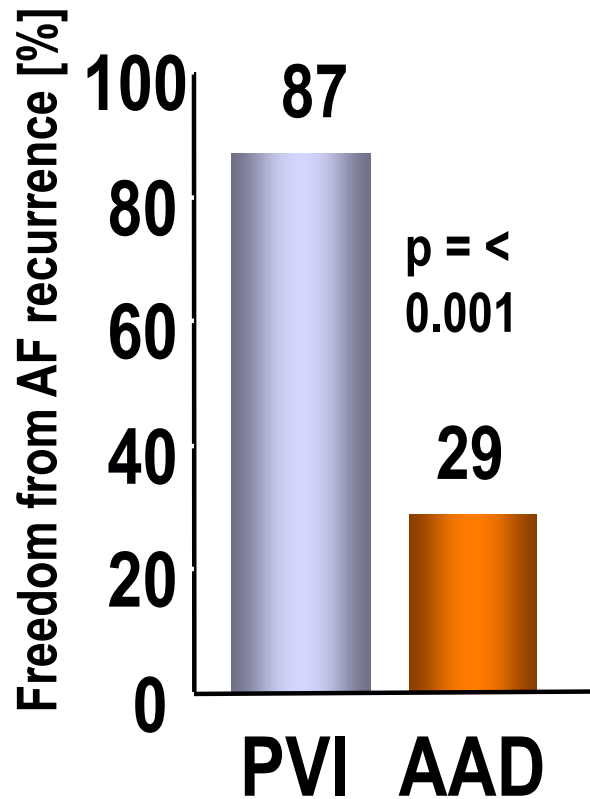


Effect of Maintaining NSR (81 %) after AF Ablation on Survival



Ablation vs. AA Therapie

APAF

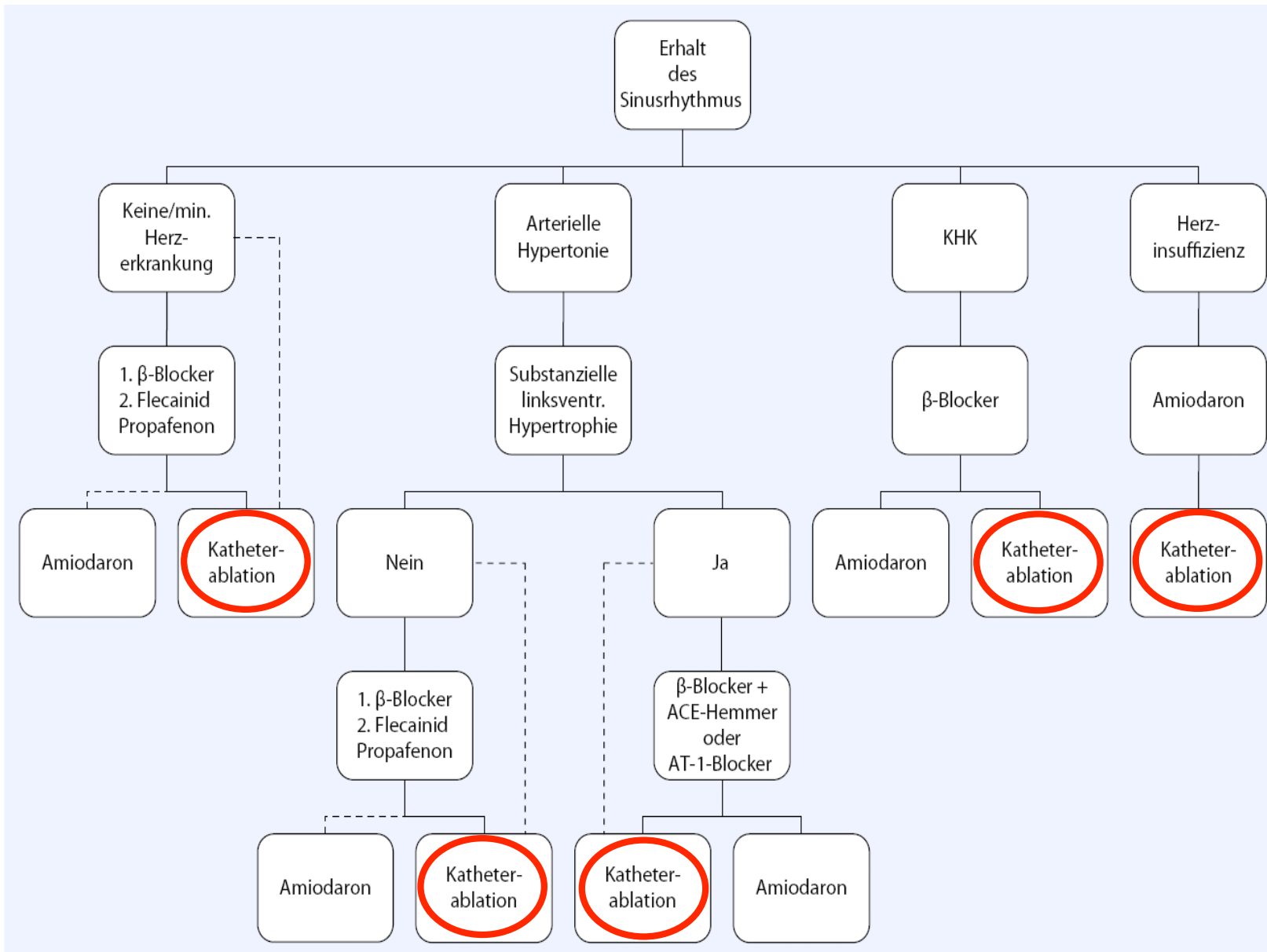


2° EP: Reduction in LA size in the PVI group

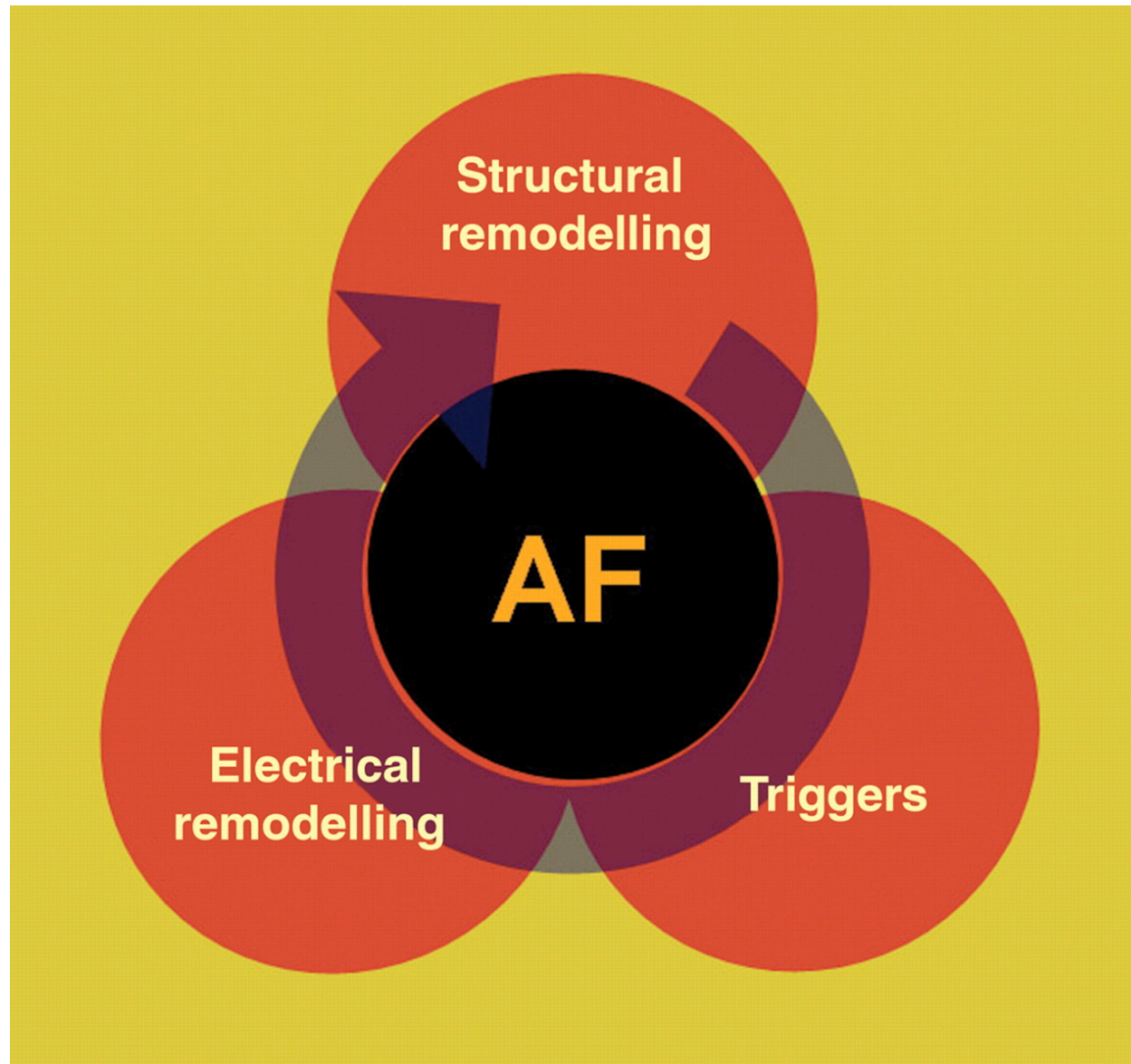
RAAFT

Study	n	AF free at 1 year	
		Ablation	AAD / control
Wazni et al, 2005 (RAAFT)	70	87%	37% (54% after the 2 nd AAD)
Stabile et al, 2005 (CACAF)	137	56%	9% (57% crossed over to ablation)
Oral et al, 2006	146	74%	4% without amiodarone; (77% crossed over to ablation)
Pappone et al, 2006 (APAF)	189	87%	29% (51% crossed over to ablation)
Jais et al, 2006 (A ⁴ study)	112	75%	7% (63% crossed over to ablation)

Rhythmus- oder Frequenzkontrolle ?



AF Mechanisms





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Indication for AF Ablation

„...I was born in sinus rhythm and
I am not willing to die in atrial fibrillation“

John Camm

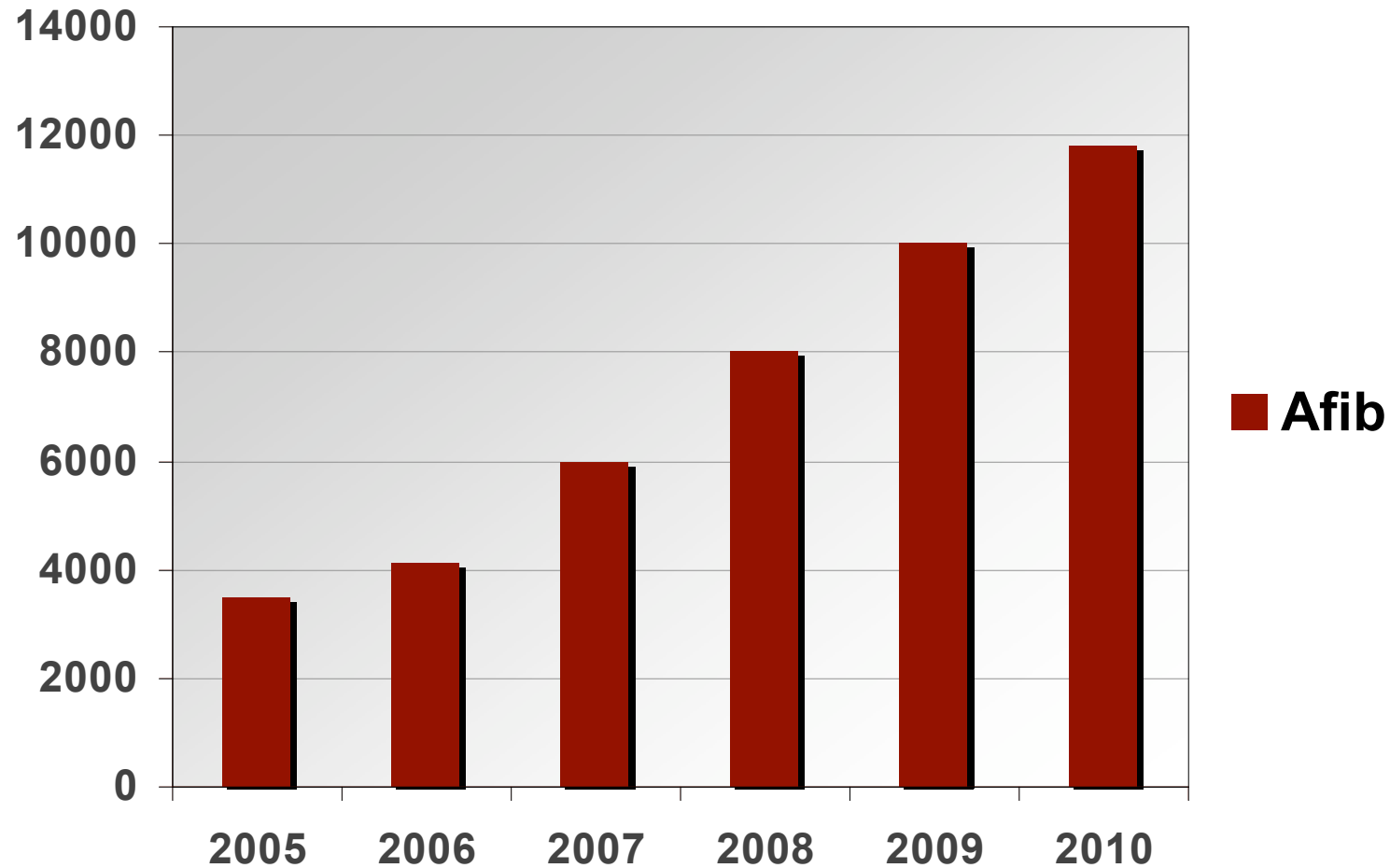


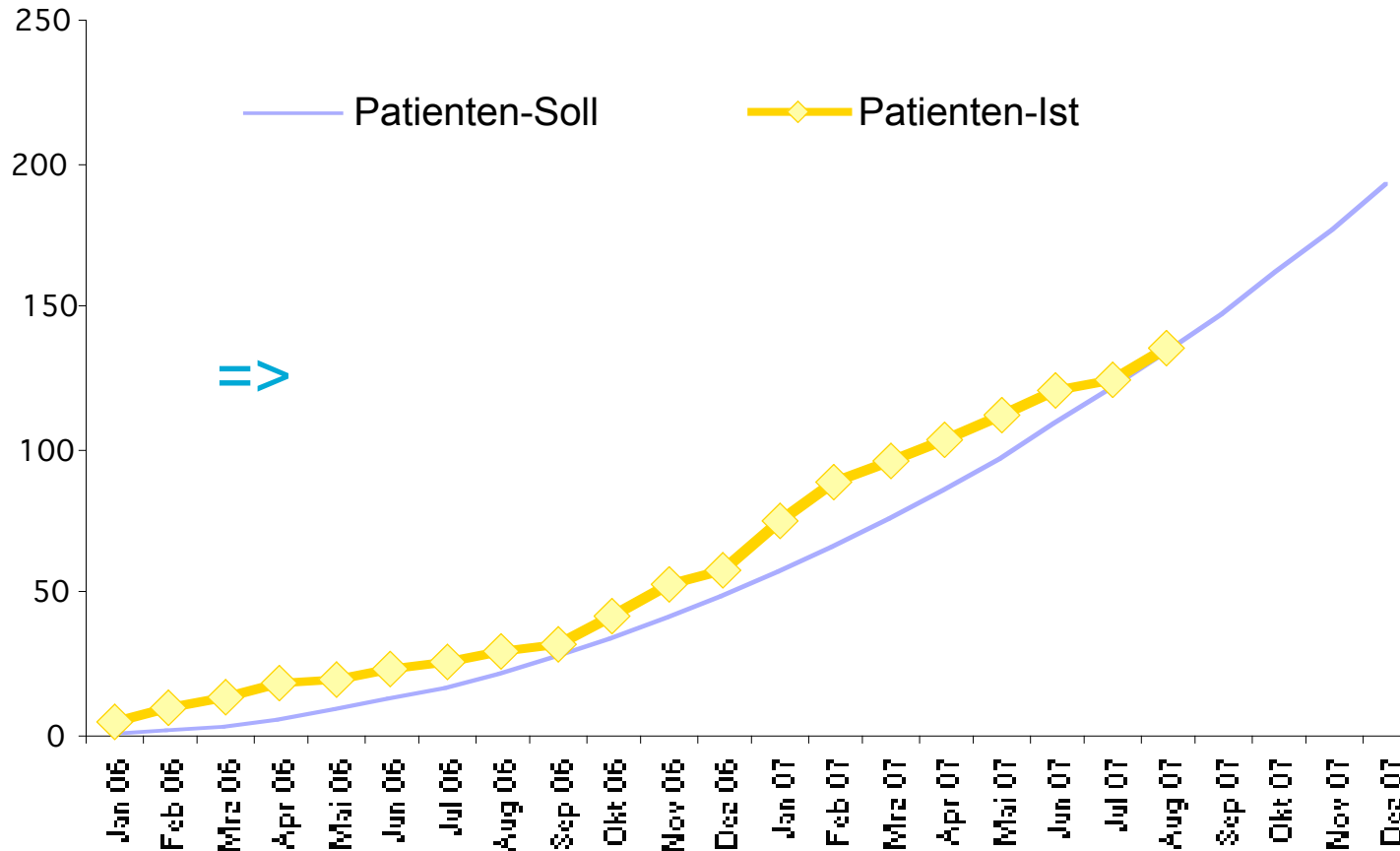
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EP Market Germany





End of inclusion phase: 3/2008



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Rhythm Control versus Rate Control
for Atrial Fibrillation and Heart Failure

Hypothese: „a rhythm-control strategy would reduce the rate of death from cardiovascular causes, as compared with rate-control strategy...in pts. with AF and heart failure“

Einschlusskriterien:

- LVEF \leq 35%
- symptomatische HI NYHA II – IV

(alternativ: NYHA I, aber LVEF < 25% und

Hospitalisierung wegen HI)

- Vorhofflimmern